

Electronic supplementary information

# Surface-controlled dissolution rates: a case study of nanoceria in carboxylic acid solutions

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## Experimental details

### Carboxylic acid structures

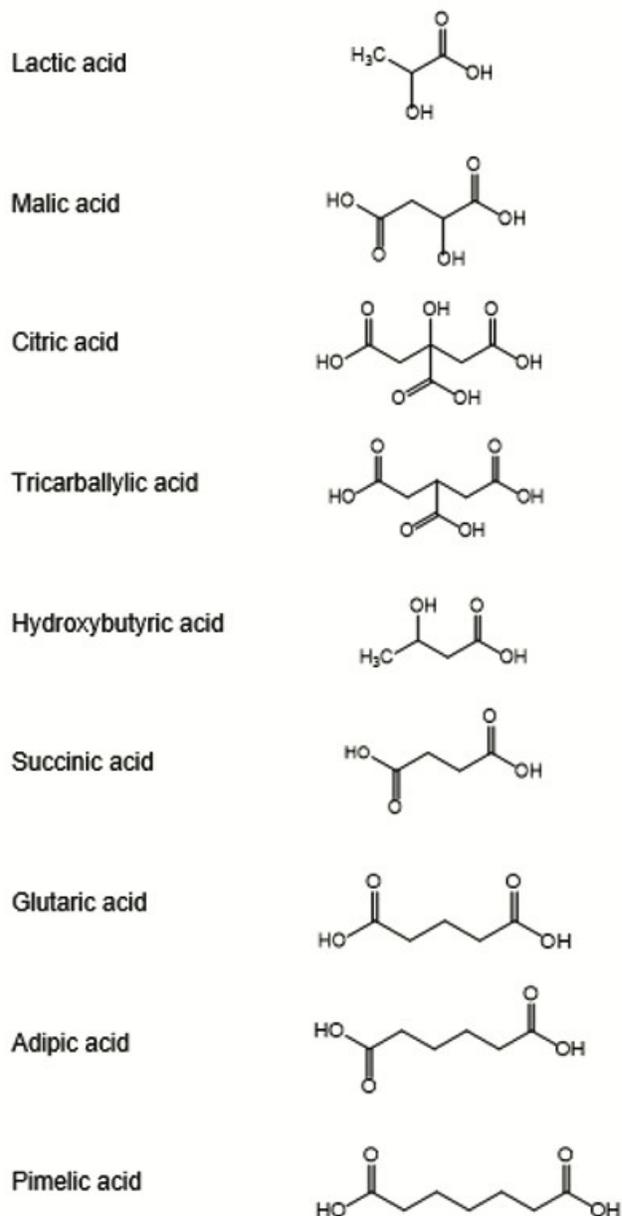


Figure S1 Structures of carboxylic acids used in the dissolution study

### Bath solutions for nanoceria dissolution study

Table S1 Bath solutions for nanoceria dissolution study. Adjusted to iso-osmotic strength by addition of sodium nitrate, using a Fiske Model 110 osmometer.

Key component	Purpose	pH	Component molarity
Water	Control	6	
Horseradish peroxidase	Control	6.1	0.67 mg + H <sub>2</sub> O <sub>2</sub> 40 μM <sup>1</sup>

<b>Ammonium nitrate</b>	Control	4.5	20 mM
<b>Acetic acid</b>	Dissolution	4.5	20 mM <sup>2</sup>
<b>Adipic acid</b>	Dissolution	4.5	110 mM
<b>Citric acid</b>	Dissolution	4.5	110 mM
<b>Glutaric acid</b>	Dissolution	4.5	110 mM
<b>DL-3-hydroxybutyric acid</b>	Dissolution	4.5	110 mM
<b>Lactic acid</b>	Dissolution	4.5	110 mM
<b>DL - Malic acid</b>	Dissolution	4.5	110 mM
<b>Pimelic acid</b>	Dissolution	4.5	110 mM
<b>Succinic acid</b>	Dissolution	4.5	110 mM
<b>Tricarballic acid</b>	Dissolution	4.5	110 mM

### Typical sampling schedule and analyses

The nanoceria added to the cassette and samples withdrawn from the cassette and bath solution were analyzed by ICP-MS for Ce content. Samples were obtained for Ce quantification for 28 to 30 weeks. A typical sampling protocol was: 1) 1 ml from the bath for Ce analysis every week, which was not replaced, 2) 75  $\mu$ L from the cassette for Ce analysis after 8, 16, and 24 weeks, which was not replaced, and 3) some samples from the bath and cassette for TEM analysis. The bathing media and dialysis cassette volumes were measured at the end of the experiment. Samples were acidified by addition of trace-metal grade concentrated nitric acid (5  $\mu$ l to 75  $\mu$ l samples, 10  $\mu$ l to 1 ml samples). TEM/STEM imaging was done on: 1) nanoceria added to the dialysis cassette and 2) nanoceria particles in the dialysis cassette, typically after 4, 8, 16, 24, and 28 weeks (25 to 45  $\mu$ l or 10  $\mu$ l when 75  $\mu$ l samples were obtained for ICP-MS). The presence of nanoparticles in the bath was determined by viewing TEM grids that had been swept through it to capture particles.

### Unsteady-state diffusion of Ce through the dialysis cassette membrane

Unsteady-state diffusion of Ce nitrate through the cassette membrane was measured to estimate its diffusivity as well as the half-life for diffusion in the system. The objective was to verify that diffusion of small Ce ligands through the membrane was much faster than the Ce dissolution process, i.e., that the Ce ion level in the bath was essentially in equilibrium with the Ce ion level in the cassette. 480  $\mu$ g Ce ion (as Ce(NO<sub>3</sub>)<sub>3</sub> hexahydrate) was introduced into a cassette in 1 ml of 110 mM citrate at pH 4.5 and dialyzed against 200 ml of 110 mM citric acid at pH 4.5. Bath samples were collected 1, 3, 6, 24, 96, 168, 336, and 504 h later for Ce quantification. The experiment was duplicated. Samples were collected 1, 3, 6, and 24 h later for Ce quantification.

Figure S2 shows data for two unsteady-state diffusion experiments. The bath concentration ratio,  $M_t/M_{inf}$ , is plotted

$$Fo = \frac{D \cdot t}{L^2}$$

versus the Fourier number (Fo) for diffusion ( $\frac{D \cdot t}{L^2}$ ), where D is the diffusivity in m<sup>2</sup>/s, t is the time in seconds, L is the membrane thickness in meters,  $M_t$  is the Ce level at time t, and  $M_{inf}$  is the Ce level at infinite time. The solid curve in Figure S2 shows an unsteady-state diffusion model<sup>3</sup>, with the diffusion coefficient fitted to both datasets using nonlinear regression. The membrane is 51  $\mu$ m thick<sup>4</sup> giving an apparent diffusion coefficient of the Ce through the membrane of  $2.9 \times 10^{-15}$  m<sup>2</sup>/s. The halftime of the diffusion process occurs at  $M_t/M_{inf} = 0.5$ , or 12.5 hours.

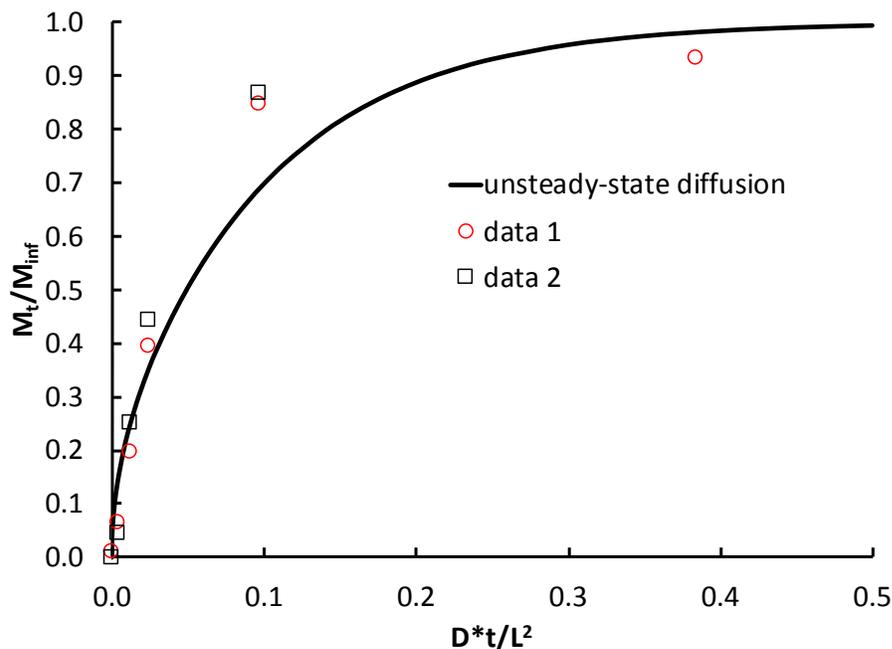


Figure S2 Unsteady state Ce nitrate diffusion from cassette into bath, pH 4.5, 37 ° C. Open circles (run 1), open squares (run 2) = data from ICP-MS Ce measurements in the bath. Solid black curve = unsteady-state diffusion model with a constant diffusivity coefficient fitted using nonlinear regression.

### Effects of dissolution on nanoceria size and shape distributions from TEM

Nanoceria size and shape distributions for the dissolution experiments were obtained from transmission electron microscope (TEM) images (JEOL 2010F). Samples were mounted dropwise on lacy carbon grids after dilution of 1:1000 followed by wicking away excess water. ImageJ was used to capture and analyze particles (see Figures 2a-b of the article).

The starting material is spheroidal or ellipsoidal in shape with clearly defined edges, so manual tracing was used to capture particles for analysis<sup>5</sup>. Quantitatively, the particles at week 0 are larger than those at week 7, which is confirmed qualitatively by TEM and dynamic light scattering (DLS). EDS confirmed the presence of cerium, oxygen, and chlorine in the sample. Chlorine is residual from the reactant required in synthesis, cerium chloride heptahydrate ( $CeCl_3 \cdot 7H_2O$ ). Area, Feret diameter, minimum Feret diameter, equivalent circular diameter (ECD), and aspect ratio descriptors were analyzed for size and shape distributions using a web-based tool for fitting distributions to data<sup>5-6</sup> (<https://shiny.as.uky.edu/curve-fitting-app/>).

### Pairwise ANOVA comparison of zero and seven week descriptor distribution means

ANOVA comparison of two descriptor distributions determines whether the means of each distribution are statistically similar to the grand mean of the combined dataset. When the statistic, the p-value, is greater than 0.05, the two distribution means are similar to the grand mean and the pair is considered to be the same. Size (area, Feret, minFeret, and ECD diameters) and shape (aspect ratio, defined as width/length, minFeret/Feret) descriptor distributions of the starting nanoceria and the nanoceria at seven weeks were compared using a web-based tool (<https://shiny.as.uky.edu/anova-app/>).

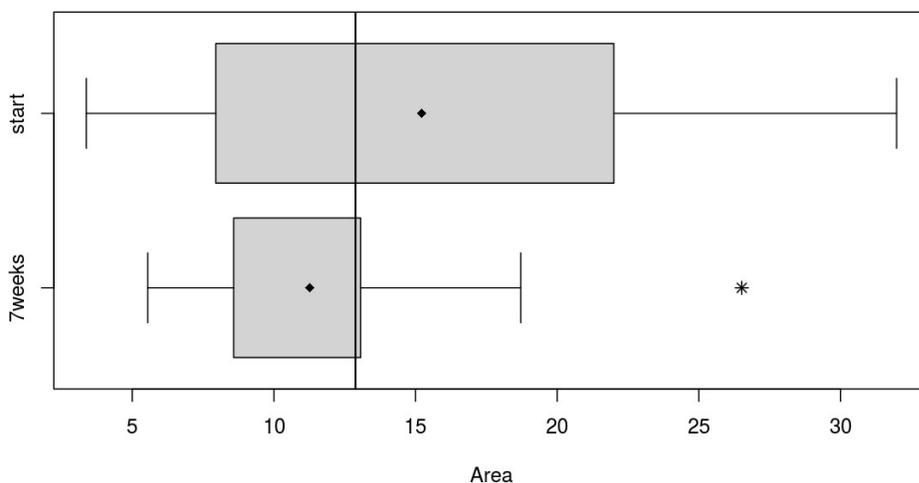


Figure S3. ANOVA boxplot of nanoceria area ( $\text{nm}^2$ ) for starting and 7-week samples. Grand mean = vertical solid line; gray boxplot = 75% of the data; black diamond = sample mean; horizontal bar = data range; asterisk = extreme point.  $P = 0.0036$ .

Figure S3 shows the boxplots for the area descriptors. After dissolution, the average nanoceria area is reduced and the area range is smaller. These data are consistent with surface-controlled dissolution. Of the five descriptors considered, only the Feret diameter descriptors passed the ANOVA test for similarity of the mean values ( $p = 0.065$ ). Figure S4 shows the Feret boxplots for nanoceria at the start of the dissolution and 7 weeks after exposure to citrate ligands. While the means are statistically similar, the seven-week dissolution sample has fewer large and small particles. Particles with dimensions less than 2 nm in diameter were not counted for this comparison.

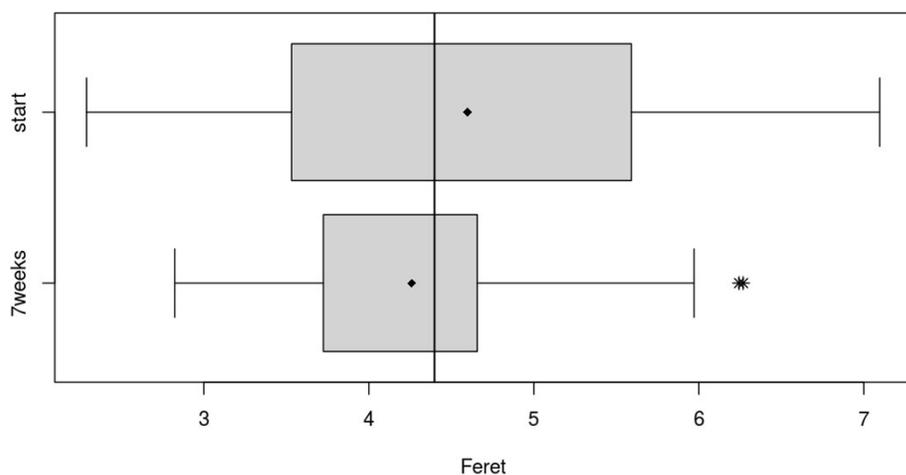


Figure S4 ANOVA comparison of Feret diameters (nm), start and seven week sample. Grand mean = vertical solid line; gray boxplot = 75% of the data; black diamond = sample mean; horizontal bar = data range; asterisk = extreme point.  $P = 0.065$ .

Figure S5 shows ANOVA boxplots of the aspect ratio (aspectR) data. The starting sample had an aspect ratio range from 0.7 to 0.97. A particle with an aspect ratio near 1 is spherical while those with lower aspect ratios might be ellipsoidal or rod-like. After seven weeks of dissolution, the aspect ratio range increased, suggesting that the dissolution process may be asymmetric. Asymmetric dissolution could occur if the dissolution rates of specific crystallite faces were different.

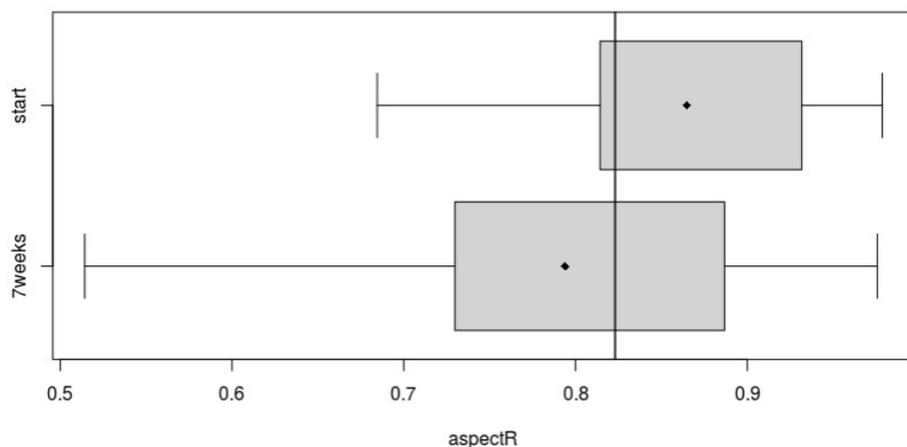


Figure S5 ANOVA boxplot of nanoceria aspect ratio for starting and 7-week samples. Grand mean = vertical solid line; gray boxplot = 75% of the data; black diamond = sample mean; horizontal bar = data range.  $P = 0.0006$

### Komolgorov-Smirnov comparison of cumulative distributions.

Komolgorov-Smirnov analysis of two cumulative distributions uses a statistic,  $D_{m,n}$ , that can determine whether they are different (see the discussion in <sup>7</sup> and its associated electronic material). The method is non-parametric and uses the distribution data directly. The computed statistic is the minimum difference between the curves for the distributions to be different. Figure S6 shows that the two distributions are different over about 10% of the Feret data range. While the ANOVA results show that the means of the distributions are similar, the Komolgorov-Smirnov analysis confirms that the distributions themselves are statistically different.

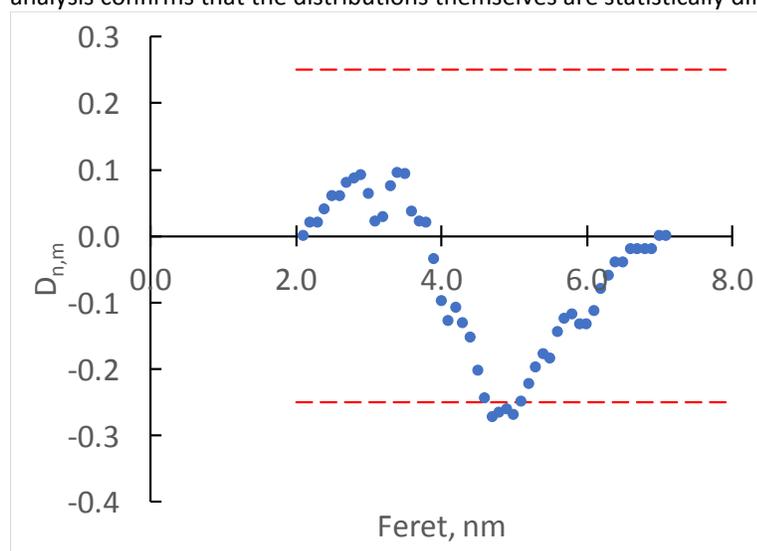


Figure S6  $D_{n,m}$  statistics ( $\pm$  as dashed red lines) compared to point-by-point differences between Feret descriptor distributions (solid blue circles for week 0 and week 7 nanocerias).

### Comparison of fitted distribution parameters

Each descriptor dataset was fitted to a normal distribution generating parameters for the mean of the distribution and the spread of the distribution. A standard error for each parameter estimate is also reported and is used to compute the coefficient of variation (the ratio of the standard error of the parameter divided by its estimate). Figure S7 shows histograms and cumulative normal distributions for the Feret diameter fitted to one of three particle datasets. The mean value for the three datasets, 4.24 nm, was used as the average starting nanoceria particle size for the surface-controlled dissolution model. Two methods were used to estimate model parameters. Nonlinear

regression often generates parameter estimates with lower coefficients of variation than the maximum likelihood method.

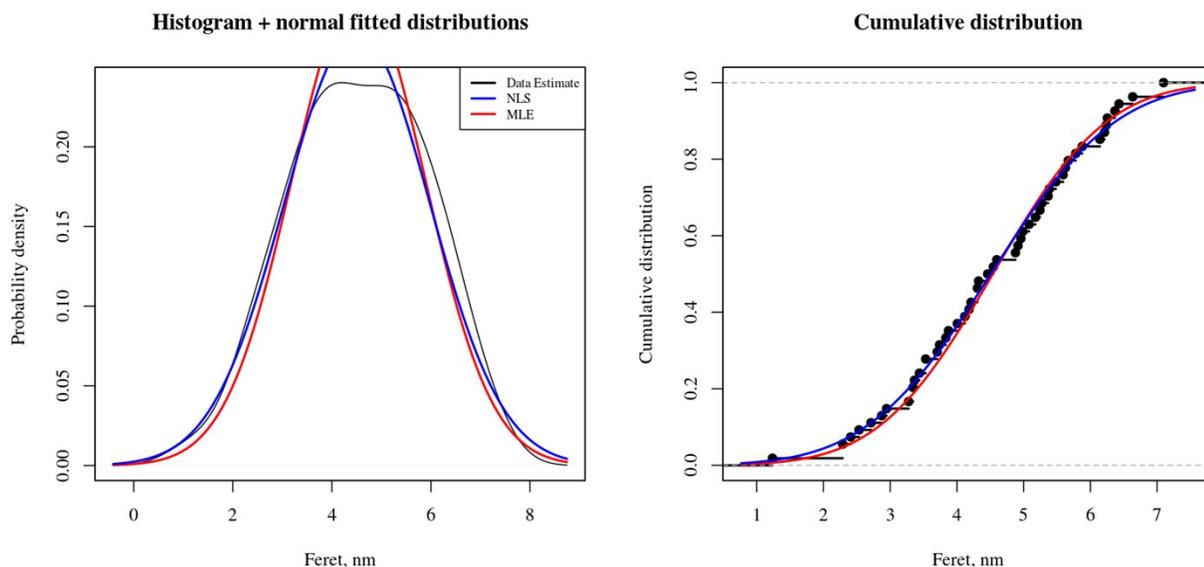


Figure S7 Histogram and cumulative distribution of Feret diameter; Black curve and points = data; blue curve = nonlinear regression fit; red curve = maximum likelihood fit

The mean parameters for normal reference models fitted for descriptor distributions are shown in Table S2 for the week 0 and week 7 citric acid bath experiments. Over this time period, the mean area decreased. The mean Feret diameter decreased moderately, such that the Feret distributions from 0- and 7- weeks are judged to have statistically similar means. The mean minFeret diameters decreased, as did the mean aspect ratio. The mean value of the ECD decreased with time, and the surface-controlled dissolution model estimates of ECD for two citric acid trials are fairly similar to the ECD mean estimated from TEM images.

Table S2 Descriptor means estimated for normal distributions fitted to measured descriptor distributions; weeks 0 and week 7 in citric acid. ECD measurements are compared to the model prediction for ECD (shown in italics) for each of two experimental trials.

Descriptor	Descriptor mean		% change in descriptor or means
	start	7-weeks	
<b>Area, nm<sup>2</sup></b>	14.4	10.9	-24%
<b>ECD, nm</b>	4.24	3.7	-12%
<b>Model-citric 1</b>		<i>3.68</i>	<i>-13%</i>
<b>Model-citric 2</b>		<i>3.78</i>	<i>-11%</i>
<b>Feret, nm</b>	4.55	4.19	-8%
<b>minFeret, nm</b>	3.89	3.28	-16%
<b>AspectR</b>	0.869	0.806	-7%

Table S3 compares descriptor fitted parameters for weeks 0 and 7. The mean and the spread are the fitting parameters of normal distributions to each descriptor<sup>5-6</sup>. The coefficient of variation ( $C_v$ , reported as a percentage) shows the quality of the fitted parameter estimate, with lower values representing less uncertainty for the estimate. For all descriptors, the coefficient of variation for the mean is less than 1%; the coefficient of variation for the spread

is less than 4%. The mean aspect ratio becomes smaller with dissolution while the spread of the distribution increases.

Table S3 Comparison of normal distribution parameters for nanoceria descriptors; starting nanoceria and nanoceria after seven weeks of dissolution

Descriptor	Week zero				Week seven			
	Mean	C <sub>v</sub> , %	Spread	C <sub>v</sub> , %	Mean	C <sub>v</sub> , %	Spread	C <sub>v</sub> , %
Area, nm <sup>2</sup>	14.4	0.94%	8.74	2.54%	10.9	0.25%	3.49	1.37%
Feret, nm	4.51	0.29%	1.47	1.47%	4.19	0.12%	0.721	1.28%
minFeret, nm	3.86	0.40%	1.38	1.86%	3.28	0.21%	0.675	1.64%
ECD, nm	4.15	0.31%	1.40	1.49%	3.70	0.10%	0.606	1.04%
Aspect ratio	0.867	0.20%	0.087	3.33%	0.806	0.29%	0.124	3.06%

### Comparison of bivariate distributions

The fitted parameter data show that nanoceria area decreased and that the particles are elongated after dissolution. Figure S8 shows bivariate plots of the Feret and minFeret descriptors for each sample. The starting sample has broader ranges of both descriptors, and good correlation between the two length descriptors, i.e., a linear relation between these two would appear to be a good model. After seven weeks, the range for both descriptors has decreased, giving clear changes in these bivariate contour plots.

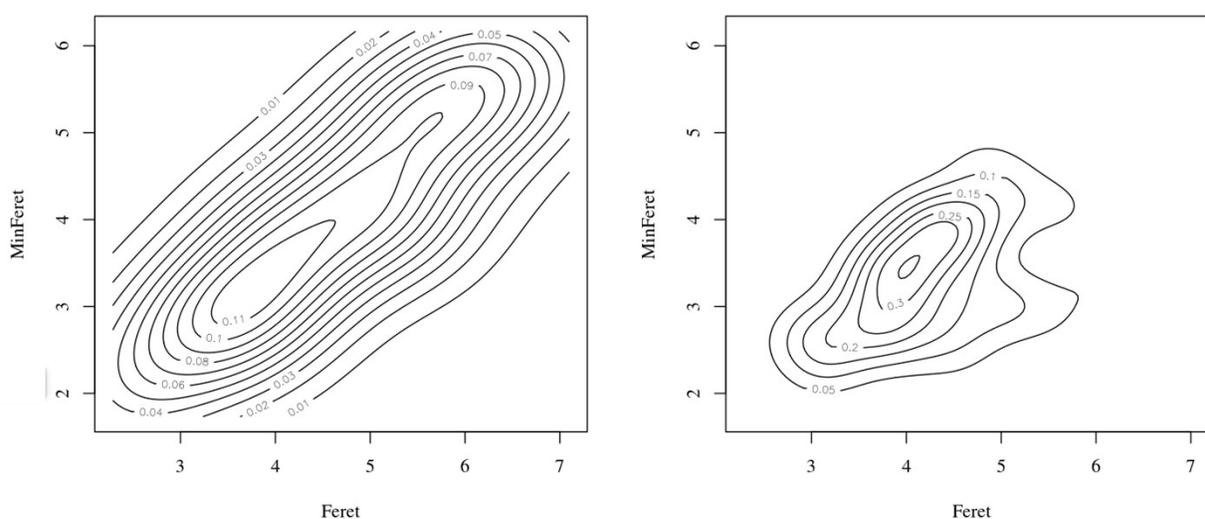


Figure S8. Feret (nm)/minFeret (nm) bivariate plots. Starting sample = left hand side; seven week sample = right hand side

Plots of the aspect ratio as a function of nanoparticle area (Figure 4 of the article) show dramatic changes in particle morphology. The average nanoparticle area has been reduced by 24% and the aspect ratio range has increased. Taken together, these changes show that nanoceria changes in size and shape during dissolution. This is consistent with other data that show some carboxylic acids adsorb preferentially on specific crystallite surface (pimelic, adipic), as discussed in the article.

After seven weeks of dissolution, this nanoceria sample has about 65% of its volume remaining using the discrete material balances for this experiment. Assuming that the volume of the average particle scales with the cube of the diameter, the ratio of average sizes should be about 87%. The ratios of the three size parameters, Feret, minFeret, and ECD, are 93%, 85%, and 88% respectively. Therefore, the discrete dissolution material balances appear consistent with the observed particle size changes.

## Discrete material balances: dissolution experiment

Discrete material balances were developed to account for Ce removal. Three types of balances were required: volume balances for the cassette and bath phases, solid nanoparticle balances for the cassette phase, and atom balances for the cassette and bath phases. With the exception of very few isolated crystallites in the size range of ~ 0.75 – 1 nm, no nanoparticles were detected in the bath solution by TEM, suggesting no nanoparticles larger than 1 nm passed through the cassette membrane or formed from the Ce ions that did pass through the membrane. Each balance was updated at each sampling event. Weekly evaporation losses were estimated by dividing the total volume loss by the total number of weeks, updating the bath volume each week. Weekly values of net solution flux between the cassette and the bath were estimated by dividing the total volume change for the cassette not attributable to removed samples by the total number of weeks, updating the cassette volume and its Ce ion level each week. Table S4 shows the variable definitions for the volume, Ce, and nanoparticle balances.

Table S4 Variable definitions for volume, Ce, and particle balances

Variable name	Definition
<b>Volume balance variables</b>	
$V^k(i)$	Volume in bath <sup>(B)</sup> ; cassette <sup>(C)</sup> . $i^{\text{th}}$ time interval (ml)
$V_{ICP}^k(i)$	Volume removed from bath <sup>(B)</sup> or cassette <sup>(C)</sup> for ICP-MS testing (ml)
$V_{EM}^c(i)$	Volume removed from cassette for EM imaging (ml)
$V_{evap}^B(i)$	Evaporation loss from bath per week (ml)
$V_{flux}^C$	Liquid volume lost or gained in the cassette per week (ml)
$\varphi^k(i)$	Volume fraction of phase k, $i^{\text{th}}$ time interval
<b>Particle balance variables</b>	
$d_1(i)$	Nanoceria particle diameter at interval $i$
$n_1(i)$	Number of Ce atoms in a nanoparticle at interval $i$
$p(i)$	Number of ceria nanoparticles at interval $i$ (in cassette)
$W_{ceria}(i)$	$\mu\text{g}$ Ce in solid nanoparticles
<b>Soluble Ce variables</b>	
$C^k(i)$	Soluble Ce concentration ( $\mu\text{g}/\text{mL}$ ) in the bath <sup>(B)</sup> or cassette <sup>(C)</sup>
$W_{Ce}^k(i)$	Weight of soluble Ce in the bath <sup>(B)</sup> or cassette <sup>(C)</sup>

The volume fractions of the cassette and bath liquid phases are:

$$\varphi^B(i) = \frac{V^B(i)}{V^B(i) + V^C(i)}; \varphi^C(i) = 1 - \varphi^B(i) \quad \text{Eq. S1}$$

At the start of an experiment, the cassette volume is 1 ml and the bath volume is 200 ml. The volume fraction of the total liquid phase that is in the bath is 200/201 or 0.995.

### Bath balances

The bath volume at the start of the  $i^{\text{th}}$  interval is that of the previous interval minus sampling losses and evaporative losses. Evaporative losses have been averaged across the entire experiment. EM samples taken from the bath are not included in the volume balance; these were acquired by sweeping an EM grid through the fluid.

System volume balance

The bath's initial and final volumes were measured. The volumetric losses from the bath were the sum of all sampling for ICP-MS analysis and evaporative losses. The evaporative loss volume was determined by setting Eq. S2b to zero.

$$\sum V_{losses}^B = V_{ICP-MS}^B + V_{evap}^B \quad \text{Eq. S2a}$$

$$V_{initial}^B - V_{final}^B - \sum V_{losses}^B = 0 \quad \text{Eq. S2b}$$

The bath volume at the start of the  $i^{\text{th}}$  interval:

$$V^B(i+1) = V^B(i) - V_{ICP}^B(i) - V_{evap}^B(i) \quad \text{Eq. S2c}$$

Ce ion balance

The  $\mu\text{g}$  of Ce ion in the bath is its concentration in the bath times the volume of the bath:

$$W^B(i) = C^B(i) \cdot V^B(i) \quad \text{Eq. S3}$$

The Ce mass balance for the bath at the beginning of interval  $i+1$  is:

$$W^B(i+1) = C^B(i) \cdot (V^B(i) - V_{ICP}^B(i) - V_{evap}^B(i)) + \phi^B \cdot \Delta W_{cerium}(i) \quad \text{Eq. S4}$$

where  $\phi^B$  is generated from Eq. S1 and  $\Delta W_{Ce}(i)$  is the mg of Ce generated (dissolved) during the time period,  $i$  to  $i+1$  (determined by the surface-controlled dissolution model fitted to the bath concentration data, Eq. 7). Most of the released Ce ions will partition to the bath phase, i.e.,  $\phi^B \sim 1$ . The ICP-MS samples are withdrawn at the end of the  $i^{\text{th}}$  interval and the evaporative loss per week is assessed at the end of the  $i^{\text{th}}$  interval. Note that water evaporation does not result in Ce loss from the system. The concentration of Ce in the bath at the new time step is:

$$C^B(i+1) = \frac{W^B(i+1)}{V^B(i+1)} \quad \text{Eq. S5}$$

Ce concentrations in the bath were measured weekly so that  $C^B(i)$  is known.

The total atoms of Ce dissolved are:

$$\Delta W_{cerium} = p(i) \cdot (n_1(i) - n_1(i+1)) \cdot \frac{M_{w,cerium}}{N_{av}} \cdot 10^6 \quad (\mu\text{g}) \quad \text{Eq. S6}$$

where  $\Delta W_{Ce}$  is the  $\mu\text{g}$  of Ce dissolved over the discrete time interval,  $i$  to  $i+1$ ,  $p(i)$  is the number of nanoceria particles in the cassette at interval  $i$ ,  $n_1(k)$  are the number of Ce atoms in the particles as predicted by Eq. 7 of the article,  $M_{w,Ce}$  is the formula weight of Ce.  $\Delta W_{Ce}$  is positive, as  $n_1(k)$  decreases as time increases.

Nanoparticle balance

Nanoparticles should be retained in the cassette per the membrane specifications and no nanoceria particles were observed in the bath samples. Therefore, no nanoparticle balance is needed for the dialysis bath. Small nanoparticles containing Ce of  $\sim 0.25$  to  $0.50$  nm were observed on the lacy carbon grid of bath samples taken for HRTEM analysis; the volume fraction of this population was very low compared to the total Ce in the bath.

### Cassette balances

Cassette volume balances

During a typical experiment, four samples were withdrawn from the cassette for ICP-MS analysis and additional samples were withdrawn for EM analysis. Final volume measurements for the cassette indicated that there were fluid fluxes in or out from the bath as well. The discrete volume balance for the cassette includes all of these factors, with the  $V_{flux}^B(i)$  term as an average weekly value across the entire experimental run time.  $V_{flux}^B(i)$  term can be positive or negative, depending on the experiment; it carries with it Ce ions, but not nanoceria.  $V_{flux}^B$  has a minor effect on the overall Ce ion balance but moderate effects on the cassette volume and the nanoparticle number balance. The cassette volume balance is:

$$V_{charge}^C - V_{final}^C - \sum V_{ICP, EM, flux}^C = 0 \quad \text{Eq. S7a}$$

$$V^C(i+1) = V^C(i) - V_{ICP}^C(i) - V_{EM}^C(i) - V_{flux}^B(i) \quad \text{Eq. S7b}$$

The right hand side of Eq. 7b is set to zero by adjusting the  $V_{flux}^B$  term.

#### Nanoparticle balances

Multiple ceria nanoparticle batches were synthesized with similar and narrow particle size distributions<sup>8</sup>. The dissolution model links the rate of dissolution to the total surface area of the particulate solid. It is convenient to compute the total surface area using two independent factors, the computed size of an average nanoparticle at the start of the interval and the number of nanoparticles in the cassette. The number of nanoparticles in the cassette is:

$$p(i+1) = p(i) \cdot \left( 1 - \frac{(V_{ICP}^C(i) - V_{EM}^C(i))}{V^C(i)} \right) \quad \text{Eq. S8}$$

The nanoparticle balance is an important one. In some experiments, the cassette lost about 40% of its nanoceria through sample extractions. These losses did not affect the assumed mechanism of dissolution based on surface area.

#### Ce ion balances

$$W^C(i+1) = C^C(i) \cdot (V^C(i) - V_{ICP}^C(i) - V_{EM}^C(i) + V_{flux}^B) + \varphi^C \cdot \Delta W_{cerium\ solid}(i) \quad \text{Eq. S9}$$

If liquid left the cassette over the course of the experiment, the efflux term is the weekly volume change times the Ce concentration in the cassette.

$$C^C(i+1) = \frac{W^C(i+1)}{V^C(i+1)} \quad \text{Eq. S10}$$

In general, the amount of Ce ion in the cassette liquid phase was only a small fraction of the total Ce in the cassette, that is, most of the Ce was in the solid nanoceria phase.

### Ce bi-ligand complexes

Table S5 shows the computed energies of formation for several Ce bi-ligand complexes.

Table S5 Energy of formation estimates for some Ce bi-ligand acid complexes

	Formation Energy, eV/Ce atom
Citric	-0.54
Malic	-0.56
Succinic	-0.63
Glutaric	-0.65
Acetic	-0.67
Tricarballic	-0.74
Pimelic	-0.74
Adipic	-0.75
Lactic	-0.94

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